REMARKS

The Examiner is thanked for the due consideration given the application. The specification has been amended to improve the language and format. A substitute Abstract is provided.

Claims 1-25 are pending in the application. The claims have been amended to improve their language in a non-narrowing fashion. Claims 13 and 14 have been amended to stand as independent apparatus claims.

No new matter is believed to be added to the application by this amendment.

The Specification

The specification has been objected to as containing informalities. The Official Action asserts that the limitation "*in vivo in situ* image" at page 3 and 5 is unclear.

The specification has been amended to recite "*in vivo* and *in situ* image," which is clear.

Also, the following definitions should be noted:

In situ means to examine the phenomenon exactly in place where it occurs, i.e., without moving it to some special medium.

In vivo refers to experimentation done in or on the living tissue of a whole, a living organism as opposed to a partial or dead one.

Also, an *in vivo in situ* image is an image obtained during an in vivo and in situ conditions. *In vivo in situ* is an expression commonly used for one of ordinary skill in the art.

It is therefore respectfully requested that the objections to the specification be withdrawn.

Claim Objections

Claims 13 and 14 have been objected for the usage of the term "*in vivo in situ* image." However, similar to as discussed above, claims 13 and 14 have been amended to recite "*in vivo* and *in situ* image," which is clear.

It is therefore respectfully requested that the objections to the claims be withdrawn.

Rejection Under 35 USC §112, Second Paragraph

Claims 1-15 have been rejected under 35 USC §112, second paragraph as being indefinite. This rejection is respectfully traversed.

The remarks in the Official Action have been considered, and the claims have been generally amended in light of the remarks.

The Official Action asserts that the term "approximately" in claim 2 renders the claim indefinite. However, as noted in MPEP 2173.05(b)(A), the term "about" (which is equivalent to the term "approximately") used to define the area of the lower end of a mold as between 25 to about 45% of the mold entrance was held to be clear, but flexible. *Ex parte*

Eastwood, 163 USPQ 316 (Bd. App. 1968). Similarly, in *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), the court held that a limitation defining the stretch rate of a plastic as "exceeding about 10% per second" is definite because infringement could clearly be assessed through the use of a stopwatch.

In this case, claim 2 recites "a numerical aperture of the focussing optics is between ***approximately*** 0.5 and 1." This recitation of an unambiguous physical parameter is thus clear and definite.

The Official Action also asserts that the term "the flux" has insufficient antecedent basis. However, claim 10 depends upon claim 9, which recites "a collected flux."

The claims are thus clear, definite and have full antecedent basis. This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Rejection Under 35 USC §101

Claims 13-25 have been rejected under 35 USC §101 as bridging two statutory classes. This rejection is respectfully traversed.

Claims 13 and 14 have been amended to stand as independent apparatus claims, which clearly fall within the aegis of 35 USC §101. Claims depending upon claims 13 or 14 have statutory basis for at least the above reason.

This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Rejection Under 35 USC §102(b)

Claims 1-25 have been rejected under 35 USC §102(b) as being anticipated by RICHARDS-KORTUM et al. (U.S. Patent 6,370,422). This rejection is respectfully traversed.

The present invention pertains to a method and apparatus for realizing a confocal *in vivo* and *in situ* image. The apparatus of the present invention is illustrated, by way of example, in Figure 1, which is reproduced below.

FIG.1

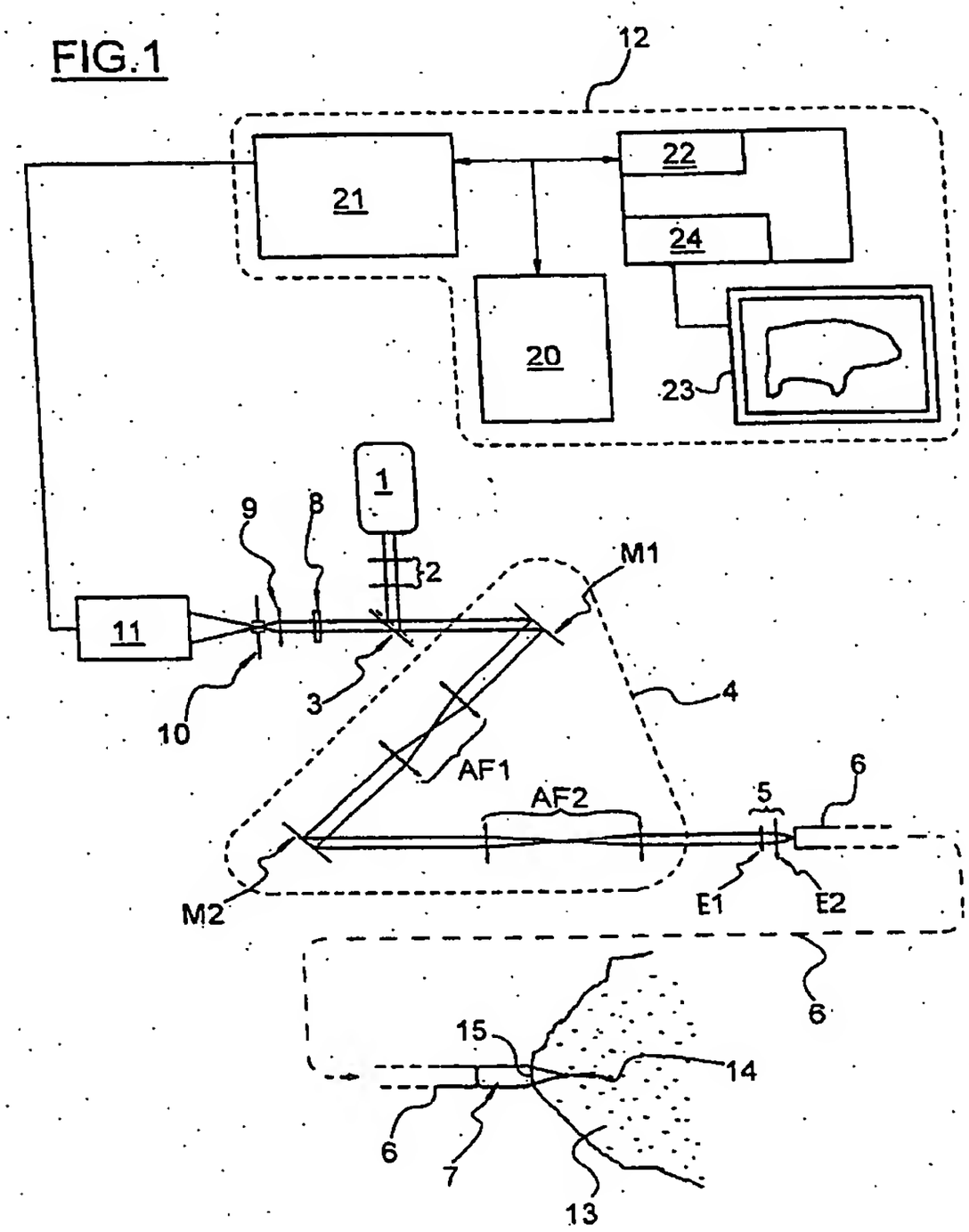


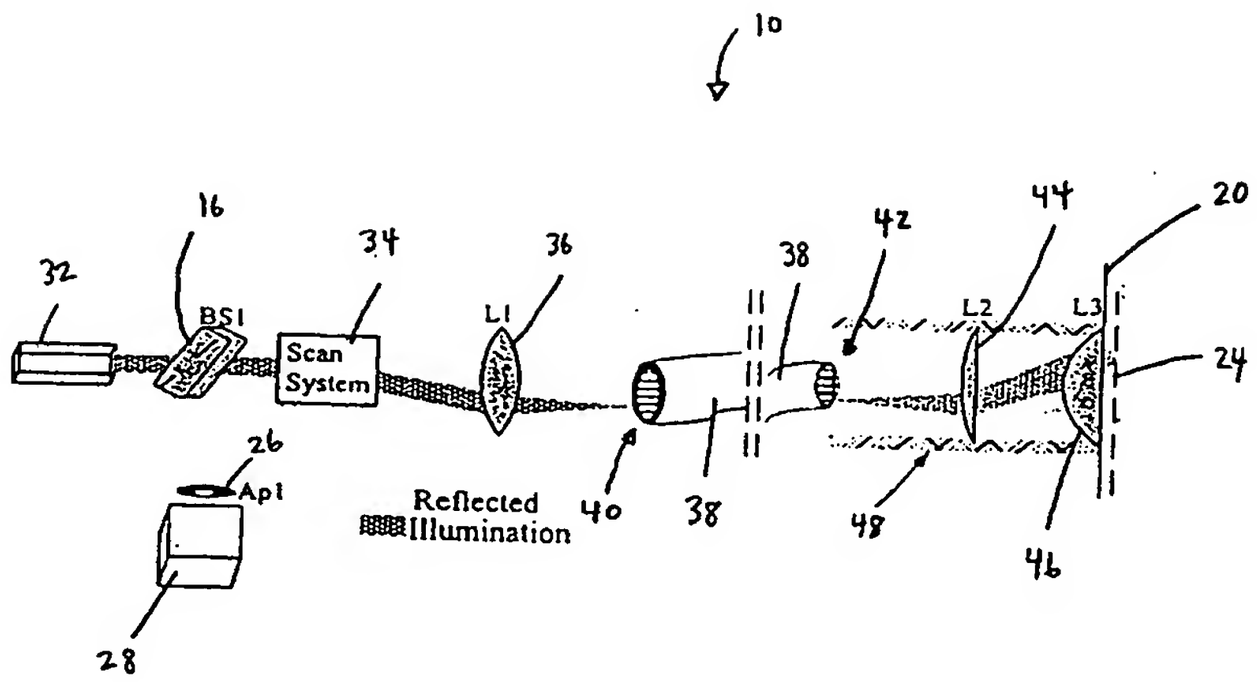
Figure 1 illustrates a light source 1, a beam shaper 2, a wavelength separator 3, a beam rejector 8, a focusing lens 9, a spectral filter 10 and a detector, which is coupled to electronic processing 12. A scanner 4 leads to a beam injector 5 connected to an image guide 6 made up of flexible optical fibers. A focusing head 7 is directed at point 14 relative to a surface 15 of specimen 13.

Independent claims 1 and 3 of the present invention recite: "the fluorescence signal is detected at a detection frequency corresponding to a minimum sampling frequency of the fibres one-by-one." Newly independent claims 13 and 14 contain analogous recitations.

RICHARDS-KORTUM et al. pertains to reflective fiber optic confocal imaging.

It should be noted that Laser Scanning Confocal Microscopy (LSCM) notably contains two techniques: 1) confocal reflection microscopy, and 2) confocal fluorescence microscopy. The present invention clearly relates to confocal fluorescence microscopy. These two techniques could be complementary but not interchangeable, as they are two different techniques.

While the present invention pertains to confocal fluorescence microscopy, RICHARDS-KORTUM et al. pertain to confocal reflection microscopy, as is clearly set forth in Figure 2 of the reference, which is reproduced below.



The Official Action (paragraph 46) asserts: "RICHARDS-KORTUM et al teach an apparatus for in situ and in vivo fibred optic confocal ***fluorescence*** imaging …" referring to column 1 lines 16-19, which states: "The present invention relates generally to the fields of optics and microscopy. More particularly, it concerns apparatus and methods for analyzing samples using fiber-optic confocal imaging techniques." There is no teaching or inference of fluorescence in that passage.

Paragraph 46 of the Official Action additionally asserts: "the source (12) emitting continuously at the excitation wavelength of at least one targeted ***fluorophore***,…" RICHARDS-KORTUM et al. at column 9, line 45 mentions a light source 12, but there is no teaching or suggestion of a fluorophore.

Paragraph 46 of the Official Action also asserts: "means (16) for separating the excitation wavelength and the ***fluorescence wavelengths;*** means for detection (28) of the

fluorescence signal..." However, there is not teaching or suggestion in RICHARDS-KORTUM et al. of fluorescence wavelengths.

That is, RICHARDS-KORTUM et al. only deals with Confocal ***Reflection*** Microscopy throughout the entire specification and drawings; see for example:

- column 4, lines 1-4,
- column 4, lines 14-21,
- column 9, lines 42-44,
- column 10, lines 40-49,
- column 10, lines 60-62, and
- Figures 1 and 2.

Furthermore, at column 2, lines 56-62, RICHARDS-KORTUM et al. clearly casts doubts on the use of fluorescence excitation on a fibered confocal microscope (Gmitro and Aziz, 1993).

RICHARDS-KORTUM et al. only discuss fluorescence at column 26, lines 30-33 and at column 10, lines 62-64: "In another embodiment, a map may be formed from fluorescence data gathered according to the above description." However, this description strictly relates to confocal ***reflection*** microscopy.

It is common knowledge that a confocal reflection microscope as described by RICHARDS-KORTUM et al. is incapable of directly being utilized for fluorescence techniques.

A fluorescence microscope is a light microscope used to study properties of organic or inorganic substances using the phenomena of fluorescence instead of reflection. In most cases, a

component of interest in the tissue is specifically labeled with a fluorescent molecule called a fluorophore. The tissue is illuminated with light of ***a specific wavelength*** which is absorbed by the fluorophore, causing this fluorophore to emit light of a ***longer wavelength*** than the absorbed light. The illumination light is separated from the much weaker emitted fluorescence through the use of a dichroic beam splitter generally associated with a rejection filter.

Fluorescence microscopy has become an important technique in the field of biology due to the high degree of sensitivity afforded by the technique coupled with the ability to specifically target structural components and dynamic processes in chemically fixed as well as living cells and tissues. On the contrary, reflection microscopy has limited applications in biomedical imaging since it provides with a strictly morphological image.

Confocal fluorescence microscopy deals with at least two different wavelengths and is intended to illuminate labeled tissue in most cases. In fluorescence microscopy, special care must be taken about:

- photobleaching, which put limits to the power of excitation
- high degree of sensitivity,
- choice of the excitation wavelength,
- choice of the targetted fluorophores

- spectral shift between excitation and fluorescence signal
- proper rejection of the excitation backscattered in the biological sample or by the optical elements of the instrument
- optimized spectral bandpass to detect enough fluorescence while minimizing achromatic constraints, and
- electronic bandpass, as soon as a rapid detection, corresponding *to in vivo* , i.e. real-time, operation is foreseen.

Thus, one realizes that components used in a fluorescence microscope are fundamentally different from that used in a reflection microscope. For example, the light source, the beam splitter and the photodetector are definitely not the same.

For the foregoing reasons, RICHARDS-KORTUM et al. fails to disclose a method or apparatus for the realization of a confocal fluorescence *in vivo* and *in situ* image.

In addition, the Official Action appears to argue that the detection means "have a pass-band whose frequency is fixed as a function of the minimum one-by-one fibres sampling frequency," referring to column 3, lines 61-67, column 4, lines 38-67, column 5, lines 1-34, column 11, lines 38-45, column 12, lines 65-67, column 13, lines 1-56 and Figures 1-31.

However, independent claims 1 and 3 of the present invention clearly states the feature that "the ***fluorescence*** signal is detected at a detection frequency corresponding to a minimum sampling frequency of the fibres one-by-one." Newly independent claims 13 and 14 set forth similar recitations. None of the art of record teaches or suggests this feature, but rather a real time scanning for a reflection signal. This feature is based on respective sampling of the fibers (according to Shannon's criterion), which makes it possible to obtain an image reconstructed point by point which effectively corresponds to each fiber. This avoids loss of information when sampling all of the fibers one-by-one while still maintaining a minimum average number of images per second. The choice of detection frequency (pass-band of the detector) as a function of this minimum sampling then allows the detection, for each fiber, of the greatest possible number of fluorescence photons.

In contrast, RICHARDS-KORTUM et al. fails to disclose this claim 1 (or 3 or 13 or 14) feature, which moreover does not apply to a reflection signal. Indeed, this feature is a limitation on the fluorescence signal, whereas RICHARDS-KORTUM et al. only deals with a reflection signal. This feature allows a fibered-laser-scanning-confocal-***fluorescence***-microscope to comply with achromatic and bandpass constraints so as to realize real time scanning and high quality images.

RICHARDS-KORTUM et al. thus fail to anticipate independent claims 1, 3 13 and 14 of the present invention. Claims depending upon these independent claims are patentable for at least the above reasons. This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

CONCLUSION

The Examiner is thanked for considering the Information Disclosure Statement filed April 18, 2005, and for making an initialed PTO-1449 Form of record in the application.

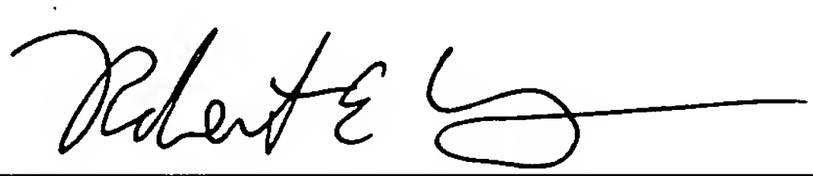
Prior art of record but not utilized is believed to be non-pertinent to the instant claims.

It is believed that the objections and rejections have been overcome, obviated or rendered moot, and that no issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowability.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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APPENDIX:

The Appendix includes the following item:

☒ - a new or amended Abstract of the Disclosure